EXHIBIT 3

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Q. Fair enough.
Doctor, I noticed, going back to your supplemental list of materials, Exhibit No. 4 --
A. Okay.
Q. -- that you were provided with reports of three of the plaintiffs other experts, Dr. Leffler, Tackett, and Lebwohl.
A. Yes.
Q. You were not provided, however, with a copy of Dr. Hutfless' report, were you, sir?
A. Hutfless?
Q. Hutfless, H-U-T-F-L-E-S-S?
A. No.
Q. Does that name even sound familiar?
A. It does not.
Q. I'll represent to you, sir, that she is an epidemiologist retained by the plaintiffs to offer opinions in this case.
A. Okay.

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Q. I'll represent to you further, Doctor, that in discussing your paper, the one we talked about in 2015 where you looked at 20 and 20, 20, 20, that she wrote that that paper does not contribute to evidence of causality or causation.
Assuming I've made the representation accurately -- I believe I have -- do you agree or disagree with that conclusion of hers?
MR. SLATER: Objection.
THE WITNESS: I think that I would agree that that paper does not make a very significant impact to the story of causation; and, really, I would also point out that, you know, those were not olmesartan enteropathy patients that we were looking at. We were specifically trying to just approximate your typical GI clinic patient who maybe has something -- they have a complaint, these

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patients had abdominal pain, but nothing serious.
So we were kind of looking to see is there a broader -- part of what we were looking for was, is there a broader range of injury either caused by olmesartan or by other ARBs, and I would agree that we did not have a striking difference amongst any of the groups.
BY MR. PARKER:
Q. Those patients, the 20, came in with complaints of abdominal pain.
A. Right.
Q. With a history of taking olmesartan.
A. Uh-hum.
Q. What made them not sprue-like enteropathy patients?
A. Well, several reasons: One is that none of the patients was dechallenged, ever, so all we would -- I think that there is a distinction to be

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drawn here between the spectrum of the variability that can be seen in olmesartan enteropathy and the more common presentations.
A very nonspecific, mild complaint like abdominal pain in a patient who happens to take olmesartan, is never taken off olmesartan, and never has any response or lack of response documented, that is not an olmesartan enteropathy patient.
If those patients had -- if the gastroenterologists in those cases had decided to take them off olmesartan and it had had some impact on them, then we could talk about them potentially being olmesartan enteropathy patients.
Q. So let me make sure I understand. These 20 patients were seen at Columbia; correct?
A. Uh-hum.
Q. They came in with abdominal pain to such a degree that they end up having an invasive procedure, an

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endoscopy; correct?
A. A common indication for a common procedure.
Q. Where snips of their tissue were taken out and studied.
A. Uh-hum.
Q. With knowledge that they were taking olmesartan; correct?
A. Uh-hum.
Q. And the GIs at Columbia said, go on home, and they didn't tell them to stop taking olmesartan?
A. To the best of my knowledge, they did not.
Q. And how long was -- did this -- how long ago were these series of 20 patients seen with abdominal pains, endoscopy results, and told -- knowing they had olmesartan -- just go on home and continue with your olmesartan?
MR. SLATER: Objection; lack of foundation.
THE WITNESS: Sorry. What was the question again?

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BY MR. PARKER:
Q. Was this relatively -- I mean, your paper is 2015.
A. Uh-hum.
Q. When were these series of 20 people seen at Columbia?
A. Oh, from what years did we get the patients, do you mean?
Q. Yes, sir.
A. I'll have to check.
Q. That's Exhibit 12 if that's helpful. Well, you can probably find it faster in your book.
(Pause.)
THE WITNESS: I don't think that we reported the years from which the biopsies were taken. I think, to the best of my recollection, it was maybe five or six years prior to the publication of this article, so --
BY MR. PARKER:
Q. And when you did your work, did you say to your colleagues, guys,

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ladies, we should go back and call these 20 people and tell them maybe they should stop taking their olmesartan?
MR. SLATER: With that same tone of voice, that -- that condescending we're a bunch of idiots voice that you're throwing out there, Bruce?
MR. PARKER: I wouldn't say it was condescending. I would say I would be incredulous if I were at Columbia and realized they hadn't been told and given your views on this. Incredulous is the tone I was trying to convey.
MR. SLATER: It's argumentative. We're almost there. Let's just take it easy.
BY MR. PARKER:
Q. Did you ever propose to your colleagues after you did this study that someone should make an effort and go back and talk to these people?
MR. SLATER: Objection.

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You can answer.
THE WITNESS: Okay. We talked about whether we thought -- whether we thought there was a reason to or not, and we decided that there wasn't and the reasons being, one, although there was a trend, it's a negative study. The P value is less than -- is more than .05, so we didn't have a definitive -- we couldn't assess causality or infer causality from something with only a trend and not a statistically significant difference --
BY MR. PARKER:
Q. But your views throughout today had been, if you had called back those 20 people still taking olmesartan, perhaps still having abdominal pain after all those years and you said stop taking olmesartan and they stopped taking it and the pain went away, that would prove causation. Right?

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A. If a patient, whether they're one of these 20 or not, had a symptom and the only change that was made was discontinuation of a medication and that resulted in the resolution of their symptom, then, yes, I would think that that is some evidence that it was causative.

Q. Let's turn to a different area.

A. Okay. I'm just going to grab some water. I'll be right back.

Q. Sure, sure. Take your time.

Doctor, I want to explore another area and if this is getting into the clinical realm and you don't feel comfortable, tell me and I'll go on.

Is it your view, Doctor, that a patient has to take olmesartan for some period of time before any GI symptoms that develop can be said to be olmesartan enteropathy if they go away when you stop taking the drug?

A. I would say that the

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literature supports that there's a pretty long lag time, on the order of months to years, before olmesartan enteropathy develops.

So I would say that maybe not in all cases, but most of the cases do involve a fairly long exposure before the syndrome develops.

And I'll say that's also in the primary context. The rechallenge data is pretty notable in that once the -- once the pump is primed for this reaction, it does appear that people get their relapses very quickly upon reintroduction of olmesartan.

Q. Before I go on to my next question, you just said something that makes me think about this: When someone is diagnosed with celiac disease and they go on a gluten-free diet and have improvement of their GI symptoms and then resume gluten in their diet, what has been your experience of the time course in which they resume having symptoms or

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an increase in the symptoms?

A. Quickly.

Q. What does that mean? Hours or days?

A. Hours to days.

Q. So in your understanding, a -- well, strike that. Let me make a foundation.

Is celiac also a delayed-type hypersensitivity reaction?

MR. SLATER: Objection.

You can answer.

THE WITNESS: No.

BY MR. PARKER:

Q. What is your understanding of the time course that the body needs to mount an attack to something through a delayed-type hypersensitivity reaction? Is it hours or is it days?

A. I don't know.

Q. Now let's go back to my question, Dr. Lagana. I want to go back to what I started to ask you to make sure I better understand your views on the

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time course that's needed to be on drug before, if GI symptoms were to develop, you might call them sprue-like enteropathy. Okay? Let me try to flesh that out for you.

A. Okay.

Q. If someone starts taking -- well, let me ask a foundational question: Is it your understanding that ARB drugs, ACE drugs, other hypertension drugs, are commonly associated with diarrhea?

A. Define "commonly."

Q. Well, do physicians who prescribe that drug recognize and see in their clinical practice that patients at times within days of starting that drug -- those drugs -- excuse me -- develop diarrhea?

A. I would think so. I don't see patients in an office, so I don't have firsthand knowledge of that, but I believe so.

Q. If someone starts taking olmesartan and with two or three days

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into taking the drug develop diarrhea, and then after two days of diarrhea, they stop the olmesartan and the diarrhea stops, is that a case of sprue-like enteropathy?

A. I wouldn't classify it that way. I would classify it as an adverse drug reaction, diarrhea, but I would not think that fits criteria for sprue-like enteropathy associated with olmesartan.

Q. Now let me go the other extreme and let's say, after two years on the drug, someone develops diarrhea and, after two days, they just stop the drug and the symptoms go away. Are those two days of diarrhea sprue-like enteropathy?

A. They had two days of diarrhea?

Q. Yeah, and then they stopped, the diarrhea goes away. So both cases, diarrhea for two days. One, it starts two years after you start the drug, the other one two days after you start the drug.

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A. Could you repeat the question, please? I'm not sure I understood.

Q. Sure. I'm trying get an understanding. You said to me -- but if I was wrong, correct me -- if someone starts taking olmesartan and two or three days into taking the drug, they develop diarrhea and after two days they stop the olmesartan and it goes away, you said, I wouldn't characterize that as sprue-like enteropathy.

A. Yes.

Q. Okay.

Now, if someone has been on the drug for two years and then develops diarrhea one day and, after two days of diarrhea, stops taking olmesartan and the diarrhea stops, does that now become a case of sprue-like enteropathy?

MR. SLATER: Objection to the form.

You can answer.

THE WITNESS: Well, in that

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hypothetical situation and those are the only facts that exist in this vacuum, I would say that that question is not entirely -- it's not entirely knowable.

BY MR. PARKER:

Q. And what is it about the person who has been taking for two years, develops diarrhea, stops the drug after two days of diarrhea, and the diarrhea goes away, what is unknowable about that case the way you look at causation to determine whether that's sprue-like enteropathy?

MR. SLATER: Objection.

You can answer.

BY MR. PARKER:

Q. What else would you have to know?

A. Okay. Let me think for a moment before I answer you.

Q. Sure.

(Pause.)

THE WITNESS: So in your

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initial premise, two days would be a very short period of time to cause an organic change to the GI tract, which is why I was pretty comfortable excluding your initial patient as an olmesartan enteropathy patient.

In the second case, two years is plenty of time for an organic change to develop. The most typical case of olmesartan enteropathy that we've seen has involved chronic diarrhea. That's not all of them. That's an example, but that's been defined as 30 days or more of diarrhea.

Two days of diarrhea is an extremely common scenario. The person might have eaten something bad. But if you showed me a biopsy done while they were having diarrhea, if it had histologic features that were suggestive of olmesartan enteropathy, and the

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patient truly stopped having those features -- those symptoms after stopping the olmesartan, I would certainly consider the possibility that they might have had early olmesartan enteropathy.
BY MR. PARKER:
Q. It is your view, is it not, sir, that the only medical intervention that's needed in someone who you will say has sprue-like enteropathy is just stop taking olmesartan and you'll have complete recovery?
MR. SLATER: Objection.
You can answer.
THE WITNESS: Okay.
MR. SLATER: I'm not sure I understood it.
THE WITNESS: Yeah, can you repeat that for me, please?
MR. PARKER: Sure.
THE WITNESS: Thank you.
BY MR. PARKER:
Q. Isn't it your view of

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causation as expressed here that if somebody has developed sprue-like enteropathy associated with olmesartan, all you need do is to tell them to stop taking the olmesartan and they will have complete remission?
A. No, I think that that's definitely mischaracterizing my statements on the topic. I will clarify, though.
MR. SLATER: He's not asked you to, actually. If he wants you to, he'll ask you to.
MR. PARKER: No, I wasn't going to because I got time problems.
BY MR. PARKER:
Q. Could you turn to reference --
A. I would like to.
MR. SLATER: Okay. I'm sorry.
THE WITNESS: First off, I'd like to know, was that question

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related to treatment or to diagnosis or both?
MR. PARKER: Treatment. I said all you need to do is to tell them to stop taking olmesartan.
THE WITNESS: Well, some of these patients come in with terrible dehydration and kidney damage, so if you don't rehydrate them, they'll die --
MR. PARKER: My example was two days of diarrhea.
THE WITNESS: Okay.
MR. SLATER: Your question was different, though, the one you just asked there. So with all due respect to him, you actually asked a broader question.
THE WITNESS: So, yes, I don't think that in every case simply holding olmesartan is the absolute only intervention that's required for those patients.
BY MR. PARKER:

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Q. Let me ask you to pull up the exhibit -- well, it's your 2016 paper.
A. The review article?
Q. Yes, systematic review.
A. Okay.
Q. Exhibit 10.
A. Okay.
(Pause.)
MR. PARKER: It might be easier to find it on the desk.
THE WITNESS: Let's see. I got it.
MR. PARKER: This is yours. That's not an exhibit.
THE WITNESS: Okay. Thank you.
BY MR. PARKER:
Q. You got it?
A. I got it.
Q. Let's go to the last page of that article. Above references -- there you go -- and do you not say, "Cessation of olmesartan results in complete

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resolution of both clinical and histologic features"?
A. I say that and that's true. I don't believe I said that that happens 100 percent of the time completely.
Q. Well, you sure don't qualify it in saying "in some patients," do you?
MR. SLATER: Objection; argumentative. Is there a question?
MR. PARKER: Yeah.
MR. SLATER: It's an argumentative question.
MR. PARKER: You do not say in this paper anywhere that only some of the people who you take off olmesartan will have complete resolution of clinical and histologic symptoms.
MR. SLATER: Objection; foundation, argumentative.
THE WITNESS: In my experience, the overwhelming majority of patients who I have

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seen the biopsies for have had complete resolution of their histologic changes.
So I've seen patients who had flat, small intestinal mucosa, who had fibrosis, who had patterns of injury that when I was in med school were associated with high mortality -- actually, collagenous sprue was recently a pretty deadly disease in a lot of patients -- I've seen patients with that histology go from that to looking totally normal by biopsy, from looking as if they just walked in the street -- walked in off the street feeling great, and that's the vast majority of cases I've seen.
I've seen very few cases that had any residual damage; and through discussion with my clinical colleagues, most of the patients that they've seen have

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had complete resolution of their symptoms and feel great after stopping olmesartan.
So what I said here, I stand by. I think it's true. Does it apply to every single patient? Probably not.
MR. PARKER: Okay.
BY MR. PARKER:
Q. So go back to my example. I'm still trying to understand what makes a case of sprue-like enteropathy and what doesn't.
If the patient has developed diarrhea after starting the drug after two days and has diarrhea for two days, how is that case of diarrhea clinically any different than the patient who's been on the drug for two years, has two days of diarrhea and stops the drug, and the diarrhea goes away?
A. Well, I want to say object to foundation, because two days -- two days would be really not the typical

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presentation of an olmesartan enteropathy patient, so -- most of these patients that we're talking about, we're not talking about two days of diarrhea.
So let me say that I think that the hypothetical situation is flawed because two days is not really a sufficient amount of time for us to think about what we believe to be a fairly uncommon entity when things like, you know, eating a bad sandwich are common and cause two days of diarrhea all the time.
So I don't like the premise of the question.
Q. Okay. You don't like the premise of the question.
Doctor, nobody gets chronic diarrhea overnight. Right?
MR. SLATER: Objection.
You can answer.
THE WITNESS: Right. Chronic diarrhea is defined as four weeks.

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BY MR. PARKER:
Q. Right. So in your view of causality, if someone has been on olmesartan, develops diarrhea, and for any reason, their spouse, their doctor, whatever, or they decide to stop taking olmesartan, you would expect them to have complete relief.
MR. SLATER: Objection.
THE WITNESS: Can you repeat that? That was a little confusing.
BY MR. PARKER:
Q. Yeah. If somebody after two years of olmesartan use develops diarrhea and, for whatever reason, their own sense or suggestion of a doctor that may have just read one of your papers, says stop using olmesartan, and the diarrhea gets better, that's what you would expect them to do, they would get better; correct?
MR. SLATER: Objection.
You can answer.
THE WITNESS: I would only

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expect that if they had olmesartan enteropathy. If they ate bad egg salad, no -- I would still expect them to get better, but it wouldn't have anything to do with the olmesartan.
BY MR. PARKER:
Q. And how would you then know that -- if they stopped taking it, after two days the diarrhea goes away, isn't that dechallenge?
A. That is dechallenge. But then there could be rechallenge. If the person said I was at a party and there was some egg salad sitting around for six hours and I ate that, and if I was that person's doctor -- and, of course, this is a clinical judgment made by the doctor, not a decision -- not a hypothetical situation made in the vacuum of a boardroom. This is a -- if we're talking about a real-world scenario, that doctor would probably say, you were at a party in Florida, the egg salad was in

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the sun for six hours, you ate it, most likely you had food poisoning. So there's a clinical judgment that goes into this.
Now, if I was that patient's doctor and the patient had just two days of diarrhea and I really -- really wanted to know if that person had olmesartan enteropathy or not, in that case, considering that the person does not fit the typical clinical description of olmesartan enteropathy, which is chronic diarrhea, I would suggest a rechallenge.
Q. Okay. But, Doctor, the only reason they don't fit the picture is because there has been somebody or decisions have been made to intervene and stop the olmesartan; correct?
MR. SLATER: Objection.
You can answer. The hypothetical's migrating, but you can answer.
THE WITNESS: There are degrees of certainty for any

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diagnosis that one makes or doesn't make. Even when you exclude something and you say it's not this, that doesn't usually mean that you're 100 percent. It means you think it's unlikely.
So if a patient had just two days of diarrhea and then discontinued olmesartan and felt better, I would not feel like the patient definitely had olmesartan enteropathy and I would not feel that the patient definitely did not.
I would consider the patient's clinical state and the rest of the patient's scenario and if it were important for the patient to be able to take olmesartan, I would rechallenge that patient and test it.
MR. PARKER: I got a few minutes before I want to stop and give myself some time after Mr.

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Slater does his questioning.
BY MR. PARKER:
Q. Doctor, we were told by letter -- I don't see it in your references -- that you were provided with some of the reports of some of the defense experts?
A. Yes, I was.
Q. And by memory, I recall Turner and Wilson being the two. Were there any others?
A. There was one other that I glanced at. Can you mention some of them?
Q. Well, there would be a Risch, a Hanson, a Popp, and a Mann. Those are the other four plus Turner and Wilson.
A. Those other names don't sound familiar. Turner and Wilson, I definitely have read.
Q. Do you know Dr. Turner?
A. We've never met. I've heard of him.

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Q. Are you familiar with the work that he has done in the field of pathology?
A. I don't have much -- I have heard his name. I know he's a respected guy. I don't know him or the specifics of his work in any great depth.
Q. Early on in response to one of my questions, you said, well, I had read these reports and I think it was in the context of you telling me you weren't sure that there was anybody -- or you weren't aware that anybody disagreed with causation until you started reading some of these reports. And they didn't, of course, change your mind.
When you read Dr. Turner's report, was there anything factual -- I'm not asking about his opinions, but factual -- that you can tell me he's just wrong about?
A. Let me take a look.
Q. Please.
(Pause.)

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THE WITNESS: Well, at the bottom of page 3, this report draws on the cases described in the Cartee paper and does directly infer that they're the same cases in Rubio-Tapia 2012, and I think that that's a baseless connection.
(Pause.)
THE WITNESS: He says all -- on page 5, the first paragraph towards the end, he says all available data suggests that seronegative celiac disease remains a far more common diagnosis than ditto even in a -- which is his phraseology for olmesartan enteropathy -- even in a tertiary referral center and so that he references DeGaetani. I would say "far more" is an overstatement of the data.
(Pause.)
THE WITNESS: Many of his opinions seem to be -- seem to

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boil down to, there are variations in presentation, therefore, this doesn't exist. It's either three things or it's nothing, and I find that to be a recurring theme in this report and I also find it to be a terribly uncompelling theme.
I think that if you look at any GI inflammatory disease, celiac disease, for instance, the classical Marsh grading allows for six different manifestations of the disease and that's not even counting complications.
So I think a frequent theme here is variability equals nonexistence and I find that to be a specious argument --
BY MR. PARKER:
Q. Okay. But I was asking about facts.
A. Okay.
(Pause.)
THE WITNESS: So I notice

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that I have left two sticky -- I have two sticky notes on here. I think -- do those need to be --
MR. PARKER: I'm not asking you to give it to me. I'm just --
THE WITNESS: All right. I just want to -- you know, I don't want to be holding anything back that's not supposed to be --
MR. PARKER: I appreciate your candor, but, no, I got only ten minutes left, Doctor, so I want to save myself five, if you could wrap it up in five minutes.
THE WITNESS: I will do my best.
(Pause.)
THE WITNESS: Well, clearly, I think he mischaracterizes my 2015 study quite -- quite badly. Talking about the P value we published of 0.34, that's a very unfair characterization, because we published that there was a

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trend towards significance in the olmesartan-exposed patients, as we said, a P value of .1, and we compared that to the P value of other -- of other ARBs or compared to matched controls for them of -- and that was .34.
So we were saying that there's a trend towards difference in the olmesartan users and no trend towards difference in the other ARB users.
So the way that Dr. Turner has picked this out and highlighted this in his report, though factually -- the facts are true, we did report that one group had P equals .34, it's a very unfair characterization of what we published.
(Pause.)
THE WITNESS: I think on the top of page 9, he also really whitewashes the rechallenges that

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have taken place in the literature, not only in Rubio-Tapia, but also in subsequent reports.
BY MR. PARKER:
Q. Rubio-Tapia didn't have any rechallenge.
A. It didn't have controlled rechallenge, meaning that it didn't have planned rechallenge, but there were rechallenges.
Q. The anecdotal report, you're talking about the two patients.
MR. SLATER: Objection; mischaracterization, lack of foundation.
THE WITNESS: I'm talking about the rechallenges which were not controlled, which were described in Rubio-Tapia.
BY MR. PARKER:
Q. Okay. 2012 paper.
A. 2012.
Q. Okay.

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A. And there are -- if we're getting on the topic of are there other rechallenges, there are rechallenges in the FDA. There are rechallenges in Theophile. There are rechallenges in Ianiro, all of which are positive.
And there are more rechallenges; and if we want to contest this point, I would be happy to go through this and point to every positive rechallenge.
Q. I was only following up on your comment about Rubio-Tapia.
A. Okay. I want to make the point that there are quite a few positive rechallenges in the literature and if you want to go into that in more depth, I'm willing to.
Q. I don't want that. I just want to hear what other -- if there were anything else in Turner's report that you believe to be factually incorrect.
A. Okay. Well, I'm on the last page.

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Q. Okay. Good news.
A. I think I would leave off with Turner's report by saying, I disagree with his conclusions. I think many of them are unfair and unfounded and I disagree.
MR. PARKER: Okay. Thank you. I'll save whatever couple minutes I have until after Mr. Slater's finished.
MR. SLATER: On my count, that's seven minutes. We're going to take a break. I have to organize my notes, so we'll take a few.
(A recess was taken from 6:32 p.m. to 7:05 p.m.)
- - -
EXAMINATION
- - -
BY MR. SLATER:
Q. Doctor, you were asked by counsel before the break about your comments in terms of your -- so the

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criticisms you had of some factual statements, some opinions from Dr. Turner's report a few moments ago. Right?
A. I was asked about that, yeah.
Q. If you were asked the same question and you were asked to go through Dr. Wilson's report, could you do the same thing and go through this as well in detail if he asked you do that?
A. Yes.
Q. Now, you were asked some questions about your 2016 article, your systematic review and whether you disclosed a, quote, unquote, conflict of interest.
Do you remember counsel asked you about that?
A. I do.
Q. Did you have an opportunity to look at the standards for what would need to be disclosed for that journal?
A. I did.

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Q. What would need to have been disclosed per the standards for disclosure of a conflict for that journal?
A. Paid testimony.
Q. Paid expert testimony?
A. Yes, paid expert testimony.
Q. Had you given any paid expert testimony in connection with olmesartan at the time this was published?
A. I had not.
Q. Did any of the authors disclose any sort of a conflict related to being a consultant to any of the people that may be involved with olmesartan? For example, if any of them were consulting for Daiichi at the time it was published, did anybody disclose anything like that?
A. No.
Q. In that article, reference 9 -- and we're talking about the Burbure article. Right? B-U-R-B-U-R-E. Right?

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A. Uh-hum.
Q. Okay.
Reference 9 in that article is what?
A. Reference 9 in that article is the Rubio-Tapia/Murray article on collagenous sprue from 2010.
Q. I might have misspoken. Let me ask you a different question: What is reference 24?
A. Okay. Basson.
Q. Were you fully aware of the Basson article when you wrote this report in this case?
A. Yes.
Q. It wasn't listed on your reliance list. Was that an oversight?
A. Yes.
Q. Okay.
Now, in this article, Burbure, on page 132, there's a reference under section 5 to establishing, quote, the diagnosis of olmesartan-induced injury. Okay?

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A. Okay.
Q. What does that mean, olmesartan-induced injury, in that article?
A. Well, that reflects the belief that we have -- that olmesartan is causing injury in this subset of patients; and as I think I said previously, until I read defense expert reports, I had not heard any controversy on that point either from my colleagues or investigators at other centers.
We have seen it in practice. We believe it. And that term is meant to plainly say it.
Q. There was some question of you, very early in the day today, and there was questioning about, quote, unquote, confused histopathology, about being confused with that.
Was that meant to suggest that somebody's making a mistake in terms of looking at histopathology as between those various entities?

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A. On the differential diagnosis?
Q. Right.
A. What I was trying to say is that some of those entities histologically can have similarities and I wasn't -- I wasn't trying to say that the pathologist would make a mistake by calling one the other. I was saying that there is histologic overlap amongst those entities.
Q. And what's the importance of clinical correlation in that context?
A. Well, clinical correlation is vital. Certainly if one is considering the diagnosis of olmesartan enteropathy, knowing that the patient was exposed to olmesartan would be pretty important.
And there are other entities on the differential that would need to be considered that also require clinical correlation. For instance, if we were talking about graft versus host disease,

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that can histologically resemble olmesartan enteropathy, but that would be in a patient who had a bone marrow transplant. So knowing the whole clinical picture is vital.
Q. Okay.
I'm going to ask you now about the Rubio-Tapia article from 2012 and I actually have the page here to save time.
A. Okay.
Q. It's okay.
I'm looking at page 737 of the article, table 3, and what is the title of table 3?
A. "Clinical features of sprue-like enteropathy associated with olmesartan."
Q. Does it say "the" clinical features of sprue-like enteropathy? Is the word "the" there in that sentence?
A. No.
Q. Your reading of this table, is that meant to be an exhaustive list of

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clinical features?
A. No. I think that these are some features, common examples of what they saw in their first 22 patients, and I certainly wouldn't take this to be exhaustive or exclusionary of other findings.
Q. The last section of that table says, "evidence of clinical and histologic improvement after suspension of olmesartan."
What's the significance of the use of the word "improvement" there?
A. Well, we've discussed this a few times today, whether improvement or resolution is necessary.
I think this is acknowledging that improvement is really, well, in some cases, the best you can hope for. Certainly you'd like to see complete resolution. You've got a sick patient.
But if you have improvement, that would be strong evidence of

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causation, if that was the only thing that changed.
Q. You were asked by counsel a few minutes ago about a hypothetical where he said a patient is assumed to have taken olmesartan for two years and then after two years develops diarrhea that lasts for two days and, after those two days are up, the person stops taking olmesartan for whatever reason.
First question on that person, would the differential diagnosis -- if you were looking back retrospectively to try to figure out what had caused the diarrhea, would the differential include olmesartan enteropathy? Yes or no.
A. Yes.
Q. If you wanted to be more sure of that at the time, when the person stopped taking the drug and then got better, would an endoscopy provide information if the person had had an endoscopy at that time?

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A. It certainly could, yeah.
Q. Could potentially.
A. Uh-hum.
Q. Would a rechallenge potentially provide important information as well if someone wanted to be sure -- you know, you got better after two days. Would giving the drug to the person again and seeing whether it recurs, would that be helpful information?
A. It would.
Q. And depending on the findings, that would be clinical information that would be factored into an ultimate diagnosis?
A. It would.
Q. Now, looking at the Basson article -- I'm just going to turn to it real quick -- and looking at page 5 of the article, and there's a statement here on the top left, "The strength of the association and the consistency with reported cases (including the long lag time between initiation of olmesartan and

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diagnosis of malabsorption) are strong arguments in favor of causality."
Is that statement of any significance to you?
A. Well, yeah, I think it's a -- it's a strong statement. They're applying the Bradford Hill criteria there, or at least some of them, and I think that -- well, they've said it quite plainly, that their findings are strong evidence in favor of causality, and I agree with that.
Q. You mentioned --
A. And by the way, if I could just mention another thing about this study --
Q. Sure.
A. -- which I don't think that we got to too specifically, when you look at the strength of the association, the relative risk of 5 or 10 as is seen after two years of therapy on olmesartan, that's a very high relative risk.
Q. And why is that significant?

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A. Well, again, getting back to the -- if we think about the Bradford Hill criteria, the strength of the association, the fact that there's a tenfold increased risk is strong.
Q. And, you know, you've mentioned the Bradford Hill criteria. Counsel had asked you if it was specifically mentioned in your report. You didn't actually name that criteria; correct?
A. That's true.
Q. Were you fully familiar with that criteria when you did your report?
A. Yeah --
MR. PARKER: Objection.
MR. SLATER: Let me ask the question again.
BY MR. SLATER:
Q. Were you familiar with the Bradford Hill criteria when you did your analysis and wrote your report in this case?
A. Yeah.

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Q. Okay.
Even though it was not named, did you take into account the factors in the Bradford Hill criteria in doing your analysis of the available information that you relied on in forming your opinion?
MR. PARKER: Objection.
MR. SLATER: You can answer.
THE WITNESS: Okay. I think that those factors are fundamental to how people in medicine think about medical science, and certainly I did think about them and I did address them, although not in the context of listing the criteria point -- on a point-by-point basis. But, yeah, I did think about them and I did try to incorporate them.
MR. SLATER: And I'm just, for the record, going to give you a list of the Bradford Hill criteria.

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BY MR. SLATER:
Q. Strength of association, consistency, specificity, temporality, biologic gradient, plausibility, coherence, experimental evidence, and analogy, is that one way to describe those criteria?
MR. PARKER: Objection.
THE WITNESS: Yes, I believe so.
BY MR. SLATER:
Q. And I'll actually -- counsel objected, so I'm going to read you -- I'm going to ask you a different question.
With regard to the Bradford Hill criteria, I'm going to list what I believe to be some of those factors and -- well, actually, you know what? I don't need to go through it again.
Are you familiar with the Bradford Hill criteria factors?
A. Yes.
Q. In analyzing, for example, the literature and your experience and

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putting that all together, did you incorporate analysis of those factors that was implicit into your analysis of this material?
MR. PARKER: Objection.
THE WITNESS: Yes.
BY MR. SLATER:
Q. Coming back to the Basson article, towards the end at the bottom of page 5, there's a statement that says, "Patients treated with olmesartan should be informed about the risk of this complication, and should be advised to seek medical attention if they experience gastrointestinal symptoms. This information should also be widely delivered to physicians of all disciplines, particularly to gastroenterologists who are faced to this new category of patients."
In the context of a question of whether there's -- whether the authors in this article had a viewpoint on causation, is that statement I just read

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to you of any significance?
MR. PARKER: Objection.
MR. SLATER: You can answer.
THE WITNESS: Okay. I don't think there's really any vagary to that statement. I think that they're expressly stating that this is a new category of patient that we're now aware of. I think that they're saying this information is important, to be widely distributed. And I absolutely agree.
The patients that we've seen at Columbia who suffered from this condition have been in terrible shape. Many have had life-threatening illness. And there's a million antihypertensives on the market. I -- you know, very rarely do you see this degree of improvement, both pathologically and clinically, with a fairly simple

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intervention.
So I think that they were clearly stating that in their opinion, this is causal and a powerful intervention.
BY MR. SLATER:
Q. Do doctors recommend that patients be warned of a risk of taking a drug if they don't think the drug causes the risk?
MR. PARKER: Objection.
THE WITNESS: Could you repeat --
MR. SLATER: Sure.
BY MR. SLATER:
Q. This statement is recommending that patients be warned of the risk of what they call this complication.
A. Uh-hum.
Q. Would doctors make a recommendation that patients be warned of the risk of a complication with a drug if they didn't think the drug caused the

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complication?
MR. PARKER: Objection.
THE WITNESS: They would not.
MR. SLATER: Now, I just have to find this one more article, and I think I left it on the desk, and then I'm done.
(Pause.)
BY MR. SLATER:
Q. I'm looking at the Histopathology article that you were asked about by Brown, et al?
A. Uh-huh.
Q. And in the article, I'm looking at the -- page 255 and there's two things that they have: They have table 1 titled "Histological Mimics of Celiac Disease" and, if you go down, it says drugs, for example, NSAIDs, olmesartan, methotrexate, mycophenolate.
Do you see that?
A. I do.
Q. And then under the materials

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and methods, it states in part, "For inclusion into the study, the following criteria had to be met," and number 3 is exclusion of a medication-related etiology such as olmesartan or chronic nonsteroidal antiinflammatory drug (NSAID) use.
Do you see what I just read?
A. I do.
Q. With regard to whether or not the authors of this study believe that olmesartan is a cause of an enteropathy that we're referring to as olmesartan enteropathy, those parts that I just read to you, what would be the significance of those sections I just read with regard to that question?
MR. PARKER: Objection.
THE WITNESS: Mind if I just take the (Indicating) --
MR. SLATER: Yeah, sure, absolutely.
THE WITNESS: Well, they say exclusion of a medication-related

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etiology such as olmesartan, so to say that it's an etiology, etiology is cause, so I would interpret this to mean that the authors of this study believe that olmesartan causes enteropathy.
MR. SLATER: Thank you.
Depending on what Mr. Parker does in his inestimable wisdom --
MR. PARKER: No, I believe the rules require me to limit my questions to your cross and there's nothing that was said that I have any other questions on.
You're done.
MR. SLATER: Thank you.
(Witness excused.)
(Deposition concluded at approximately 7:23 p.m.)

CERTIFICATE

I HEREBY CERTIFY that the witness was duly sworn by me and that the deposition is a true record of the testimony given by the witness.

It was requested before completion of the deposition that the witness, STEPHEN M. LAGANA, M.D., have the opportunity to read and sign the deposition transcript.

____
KIMBERLY A. CAHILL, a
Federally Approved Registered
Merit Reporter and Notary Public
Dated: February 9, 2017

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After doing so, please sign the errata sheet and date it.

You are signing same subject to the changes you have noted on the errata sheet, which will be attached to your deposition.

It is imperative that you return the original errata sheet to the deposing attorney within thirty (30) days of receipt of the deposition transcript by you. If you fail to do so, the deposition transcript may be deemed to be accurate and may be used in court.

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ACKNOWLEDGMENT OF DEPONENT

I,____________________, do hereby certify that I have read the foregoing pages, 1 - 418, and that the same is a correct transcription of the answers given by me to the questions therein propounded, except for the corrections or changes in form or substance, if any, noted in the attached Errata Sheet.

____
STEPHEN M. LAGANA, M.D.   DATE

Subscribed and sworn
to before me this
_____ day of ______________, 20____.
My commission expires:_______________

____
Notary Public

LAWYER'S NOTES

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